Do Electronic Cigarettes Assist Motivated Smokers With Quitting?: A Secondary Analysis from a Community-Based Study

Honors Research Thesis

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ABSTRACT

Objective: This study investigated the association between electronic cigarette, or e-cigarette, use after cessation treatment and tobacco abstinence at 12 months. It also examined characteristics of e-cigarette users and reasons for use.

Methods: A longitudinal observational secondary analysis of self-reported e-cigarette use among adult Appalachian smokers enrolled in a tobacco dependence treatment trial (n=217) was conducted. Data were collected at baseline, 3, 6, and 12 months following treatment.

Results: One in five participants reported using e-cigarettes post-treatment. Baseline sociodemographic and tobacco-related characteristics did not differ by e-cigarette use. Reasons participants cited for e-cigarette use included help in quitting, help in cutting down on cigarettes, and not as bad for health. Significantly fewer e-cigarette users than non-users were tobacco abstinent at the 12-month follow-up (4.7% vs. 19.0%, p=0.021).

Conclusions: Among adult Appalachian smokers enrolled in tobacco cessation treatment, those that used e-cigarettes post-treatment were less likely to be tobacco abstinent after 12 months. Additional high quality studies are needed to determine the effects of electronic cigarette use on long-term abstinence.

Key Words: Electronic Cigarettes, E-Cigarettes, Cessation, Appalachia

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INTRODUCTION

Tobacco use is the most preventable cause of disease and death in the United States[1], yet in 2014, an estimated 16.8% of U.S. adults (18+) smoked cigarettes[2]. The majority of U.S. adult smokers want to quit[3] and many are turning to electronic cigarettes, also known as e-cigarettes and e-cigs, as an alternative to smoking. E-cigarettes are battery-operated devices that deliver nicotine, flavor, and other chemicals through an aerosol that is inhaled[4].

E-cigarettes have rapidly increased in popularity since their introduction to the United States market in 2007[5]. The Food and Drug Administration (FDA) does not currently regulate e-cigarettes or endorse them as a strategy for quitting[4], yet e-cigarettes have been marketed as cessation aids that are less harmful than traditional cigarettes[6]. Reported reasons for e-cigarette use among smokers include assistance to help quit or reduce smoking, reduced health risks, and maintenance of smoking in places where cigarettes are restricted[7-10].

About one in five current cigarette smokers report e-cigarette use some days and 3.7% report daily use[7]. Among smokers, those who ever used e-cigarettes are more likely to be white[8,11] and young adults[9,11]. In terms of tobacco-related characteristics, e-cigarette users have been found to have a higher motivation to quit and a higher quitting self-efficacy[12], use more quit methods (i.e. NRT), and are more nicotine dependent[13], more likely to have made a quit attempt in the past year and more likely to live and/or work with other tobacco users than non e-cigarette users[8].

Two clinical trials have examined the efficacy of e-cigarettes as a cessation aid. The first, a randomized controlled trial conducted in New Zealand found that e-cigarettes are

modestly effective at helping current smokers quit, but superiority of e-cigarettes over the nicotine patch was not found[14]. The second trial was conducted in Italy and demonstrated that among smokers not intending to quit, e-cigarette use decreased cigarette consumption[15].

A few observational studies have likewise found that e-cigarette use helps smokers quit or reduces cigarette consumption. A cross-sectional study in the UK found that among adults smokers who had made a previous quit attempt in the past year, e-cigarette users were more likely to report abstinence than those who used NRT bought over-the-counter (OR, 2.23; 95% CI 1.70-2.93) or no aid (OR, 1.38; 95% CI, 1.08-1.76)[16]. Other studies have noted that e-cigarettes reduced the urge to smoke[14, 17-19] and aided in reducing cigarette consumption [20-21].

In contrast, a meta-analysis of five population-based studies noted that e-cigarette use was associated with significantly lower odds of smoking cessation (OR, 0.61; 95% CI, 0.50-0.75). Three of the studies in this meta-analysis did not control for nicotine dependence and the authors proposed that possibly those who use e-cigarettes are more nicotine dependent and experience greater difficulty quitting in general[22]. A recent random effects meta-analysis of twenty studies likewise found that the odds of quitting cigarettes were 28% lower in those who used e-cigarettes compared with those who did not use e-cigarettes (OR, 0.72; 95% CI 0·57-0·91) [23]. This meta-analysis included studies of all smokers using e-cigarettes and studies of only smokers interested in quitting. The association between e-cigarette use and cessation did not differ between study characteristics. Importantly, this study concludes that e-cigarette use is associated with less quitting.

Only a few studies have investigated e-cigarette use among smokers who are trying to quit. Vickerman et al. reported that among state tobacco quit-line callers, e-cigarette users had a significantly lower 30-day point prevalence abstinence rate at the 7-month follow-up compared with never users[8]. Similarly, among patients with cancer who were enrolled in a tobacco cessation study, e-cigarette users were twice as likely to be smoking at the time of follow-up as nonusers[24]. In a study among participants enrolled in a web-based smoking cessation trial, e-cigarette use was negatively associated with 3-month abstinence, but became insignificant when adjusted for use of other cessation aids[13].

There is a lack of scientific consensus on the impact of electronic cigarette use on tobacco cessation. While randomized controlled trials have found that e-cigarettes help smokers quit, observational studies and meta-analyses have found the opposite. Moreover, observational studies in the UK have found that e-cigarette users are more likely to quit, while in the United States e-cigarettes are associated with less quitting. More research is clearly needed.

However, regulatory restrictions in the United States make it difficult to conduct randomized controlled trials to determine the efficacy of e-cigarette devices. At present, there is no publically available data for e-cigarette manufacturing, design or preclinical studies that are suitable for meeting the requirements of an Investigational New Drug application[25]. As such, testing the efficacy of e-cigarettes through randomized controlled trials cannot occur. Thus, public health experts and clinicians increasingly rely on findings from observational studies when making recommendations to current smokers about the effectiveness of e-cigarettes in promoting cessation.

In this paper, we describe e-cigarette use among Ohio Appalachian adults who want to quit smoking and are enrolled in a tobacco cessation treatment trial. The purposes of this secondary analysis were to 1) examine sociodemographic and tobacco-related characteristics associated with e-cigarette use post-treatment, 2) describe reasons for e-cigarette use at 3, 6, and 12 months, and 3) determine the association between e-cigarette use post-treatment and biochemically confirmed 7-day point prevalence tobacco abstinence at 12 months.

METHODS

Study Overview

A secondary analysis was conducted using data obtained during a tobacco cessation treatment trial that was implemented in 12 federally designated Ohio Appalachian counties[31]. Six counties each were randomly assigned to one of two study conditions. Both conditions included standardized cognitive-behavioral counseling and free nicotine replacement therapy (NRT) in the form of a daily 21 mg patch for 8 weeks, as recommended by the US Public Health Service *Treating Tobacco Use and Dependence* guideline[26]. Smokers in one condition received face-to-face counseling from trained community health workers while participants in the other condition were referred to the Ohio Tobacco QUIT LINE. Data were collected at baseline and 3, 6, and 12 months following treatment and all participants were given an incentive in appreciation of their participation in the study. The study, approved by the university's Institutional Review Board, was conducted in three waves (2010-2014), with one-third of the face-to-face and one-third of the quit-line counties included in each wave.

Procedure

Recruitment occurred at a variety of community sites within each county that were geographically and socioeconomically distributed. Eligibility criteria included: 1) age 18 years and older; 2) current self-reported use of a combustible tobacco product on a daily basis; 3) resident of one of the 12 participating counties; 4) absence of clinical condition that contraindicated use of over-the-counter NRT; 5) if female, non-pregnant, as confirmed by urine human chorionic gonadotropin test; 6) willing to participate in study protocol; and, 7) able to provide written informed consent. A trained county interviewer contacted potential participants who were eligible and administered a face-to-face questionnaire.

Sample

Participants from the face-to-face and quit-line conditions were combined for this secondary analysis. Initial data collection started in November 2010; however, items to assess e-cigarette use were added to the existing surveys in April 2012 due to the increasing widespread marketing of e-cigarette products. This paper reports on the subset of the sample that completed baseline surveys from April 2012 to October 2013 and is restricted to only those participants who provided complete answers to use of other tobacco products, including e-cigarettes, at baseline, 3, 6, and 12 months (n=217).

Measures

Sociodemographic and tobacco-related characteristics were collected in the baseline survey questionnaire. Sociodemographic characteristics were comprised of age, gender, race, education, poverty level, self-rated health and health insurance status. Smoking variables included years smoked, age started smoking, number of cigarettes smoked per

day, and Fagerström Test for Nicotine Dependence (FTND)[27]. Quitting variables assessed number of previous quit attempts, use of quitting resources in the past, the Decisional Balance Scale for Smoking[28], confidence to quit, and Quitting Self-Efficacy Score[29]. Smoking policies included indoor home smoking rules (i.e. allowed anywhere inside the home, allowed in some places or at sometimes, not allowed anywhere inside the home) and whether a worksite smoking policy existed.

Those who reported e-cigarette use were asked about their reasons for use at every time point. Six categories of reasons were given: 1) they may not be as bad for your health; 2) they taste better; 3) they make it easier for you to cut down on the number of cigarettes you smoke; 4) so you can smoke in places where smoking regular cigarettes is banned; 5) they may help you quit; and, 6) they are cheaper. Participants were instructed to indicate all reasons that applied.

The main exposure variable of interest was e-cigarette use post-treatment. At 3, 6 and 12 month follow-ups, participants were asked if they used any kind of tobacco other than cigarettes in the past 7 days. If they answered yes, they were asked if they currently use e-cigarettes every day, some days, or not at all. The variable, "e-cigarette use post-treatment" was defined as self-reported past 7-day e-cigarette use (every day or some days) at 3, 6, and/or 12 months.

The primary outcome measure was 7-day point prevalence abstinence from tobacco (not including e-cigarettes) at 12 months post-treatment. Abstinence was defined as self-report of no tobacco use in the past 7 days as confirmed by a saliva cotinine concentration of <15 ng/mL, or by expired air carbon monoxide level of < 8 parts per million if

participant was using NRT or e-cigarettes[30]. Seven-day point prevalence tobacco abstinence was also determined at 3 and 6 months.

In addition to baseline characteristics, other potential confounders included total number of in-person counseling visits and number of patches used (face-to-face condition) and number of calls to the quit-line and number of weeks of patches received (quit-line condition).

Statistical Analysis

The data were analyzed in STATA. Sociodemographic and tobacco-related characteristics were compared between those who used e-cigarettes post-treatment and those who never used e-cigarettes post-treatment. Means and t-tests were used for continuous variables and percentages, chi-square tests and Fisher's exact tests were used for categorical variables. No correction was made for multiple comparisons, but the p-values are provided for descriptive purposes.

For the primary analysis, a Fisher's exact test assessed the association between use of e-cigarettes post-treatment and 12-month point prevalence tobacco abstinence. A mixed effects logistic regression analysis evaluated the impact of potential confounders and the impact of within county correlation. These models indicated that the within county correlation on the outcome was zero, so the presented analyses utilize methods for independent data.

RESULTS

Among the 217 participants who provided complete data, approximately one in five (19.8%) reported e-cigarette use post-treatment. The percentage of e-cigarette users generally increased over time: 7.8% at 3 and 6 months and 12.0% at 12 months.

Characteristics of E-cigarette Users

Baseline sociodemographic characteristics were not generally different between e-cigarette users and non-users post-treatment (Table 1). The majority of e-cigarette users were 25-54 years old (53.5%), female (76.7%), and white (97.6%). More than half of e-cigarette users had more than a high school degree or General Educational Development (GED) (58.1%). Approximately 13% lived below the 100% federal poverty level and 23% did not have health insurance. These characteristics were similar to the characteristics of non-users and the sample as a whole[31]. Some difference was found between e-cigarette users and non-users in self-rated health with 51% of e-cigarette users reporting fair or poor health, as compared to 30% among never users (p=0.020).

Table 1. Sample baseline sociodemographic characteristics of smokers enrolled in a tobacco cessation treatment trial by use of e-cigarettes post-treatment (n=217).

	Ever use of e-cig post-treatment (n=43)	**Never use e-cig post-treatment (n=174)**	***p* value**
Age, %			
18-24	2.3	3.5	0.59
25-54	53.5	61.5	
≥ 55	44.2	35.1	
Gender, %			
Female	76.7	68.4	0.28
Race, %			
White	97.6	94.2	0.70
Other	2.4	5.8	
Appalachian Status, %			
Appalachian	32.6	43.1	0.39
Not Appalachian	8.1	50.6	
Don't Know	9.3	6.3	
Education, %			
Less than High School (HS)	16.3	8.7	0.19
HS/GED	25.6	37.0	
More than HS/GED	58.1	54.3	
Poverty level, %			
Below 100% poverty	16.7	15.0	0.79
Self-rated health, %			
Excellent, very good	14.0	29.9	0.020
Good	34.9	40.2	
Fair, poor	51.2	29.9	

Smoking history variables did not differ significantly by e-cigarette use post-treatment (Table 2). On average, e-cigarette users smoked cigarettes for 31 years and started smoking around age 17. They smoked approximately 20 cigarettes/day. E-cigarette users on average showed moderate nicotine dependence, based on FTND scores. E-cigarette users did not differ from non-users in their nicotine dependence.

There were likewise no associations between baseline quitting history variables and e-cigarette use (Table 2). In the past 12 months, on average, e-cigarette users attempted to quit one time for at least 24 hours. Approximately three-quarters of e-cigarette users had used resources in the past to aid in quitting (i.e. NRT, other medication, quit-lines, community or internet programs, self-help materials, and healthcare providers). On a scale from 1 to 10 (1 = not at all confident and 10 = extremely confident) e-cigarette users on average scored 7 in their confidence to quit smoking.

Possible differences were found regarding smoking policies (Table 2). While 56% of e-cigarette users were allowed to smoke anywhere inside the home, only 39% of non-users had this same rule (p=0.068). Fewer e-cigarette users had a smoking policy at work (67% vs. 85%, p=0.10). However, these differences were not statistically significant.

Table 2. Sample baseline tobacco-related characteristics of smokers enrolled in a tobacco cessation treatment trial by use of e-cigarettes post-treatment (n=217).

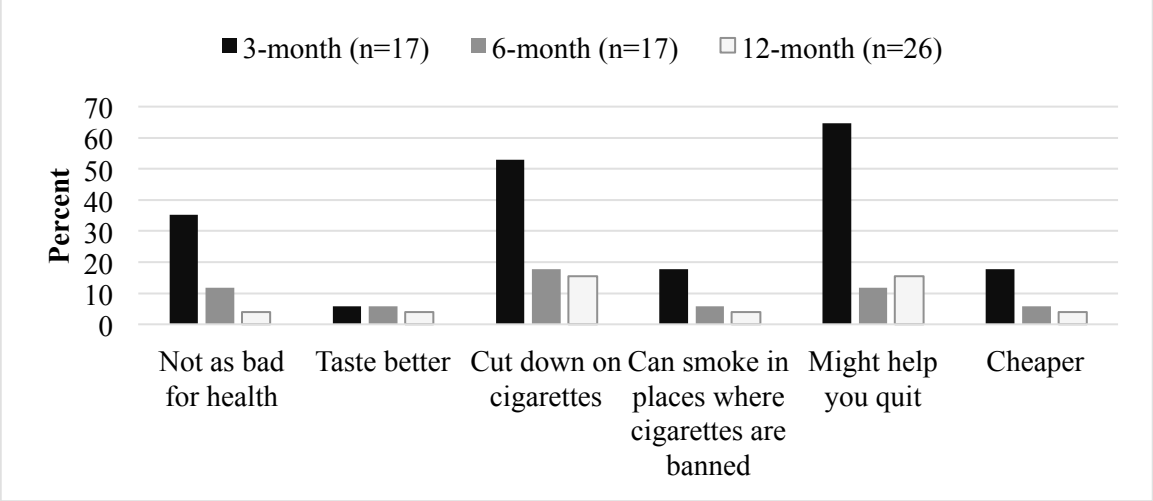
	Ever use of e-cig post-treatment (n=43)	**Never use e-cig post-treatment (n=174)**	***p* value**
Years Smoked, Mean ± SD	31.2 ± 14.9	30.8 ± 14.1	0.87
Age Started smoking, Mean ± SD	16.9 ± 6.5	17.9 ± 6.6	0.38
Cigarettes per day, Mean ± SD	22.0 ± 14.2	21.2 ± 9.7	0.67
Fagerström score, Mean ± SD	5.7 ± 1.9	5.1 ± 2.3	0.18
Quit attempts, past 12 mo, Mean ± SD	1.1 ± 1.4	1.6 ± 3.6	0.39
Used resources in past, %			
Yes	76.9	77.2	0.97
Used NRT in past, %			
Yes	58.1	50.6	0.37

Decisional Balance Scale for Smoking (pros-cons), Mean ± SD	-0.37 ± 3.2	-0.32 ± 2.9	0.92
Confidence can quit, Mean ± SD	7.3 ± 1.8	7.1 ± 2.0	0.53
Quitting self-efficacy: positive/social, Mean ± SD	10.5 ± 3.1	10.5 ± 2.7	0.97
Quitting self-efficacy: negative/ affective, Mean ± SD	12.2 ± 3.0	12.7 ± 2.2	0.19
Quitting self-efficacy: habit/addictive, Mean ± SD	9.8 ± 2.3	10.1 ± 2.3	0.46
Indoor home smoking rule, %			
Allowed anywhere inside the home	55.8	39.1	0.07
Allowed in some places or at sometimes	18.6	35.6	
Not allowed anywhere inside the home	25.6	25.3	
Smoking policy at work, n=100, %	(n=16)	(n=84)	
Yes	66.7	84.5	0.10

Reasons for E-cigarette Use

At every follow-up, the top three reasons for e-cigarette use were: 1) help in quitting; 2) help in cutting down on cigarettes; and, 3) not as bad for health (Figure 1). Interestingly, the reported reasons for use diminished over time. For example, while 53% of e-cigarette users reported that "they make it easier for you to cut down on the number of cigarettes you smoke" at 3 months, only 18% and 15% reported this reason at 6 and 12 months, respectively.

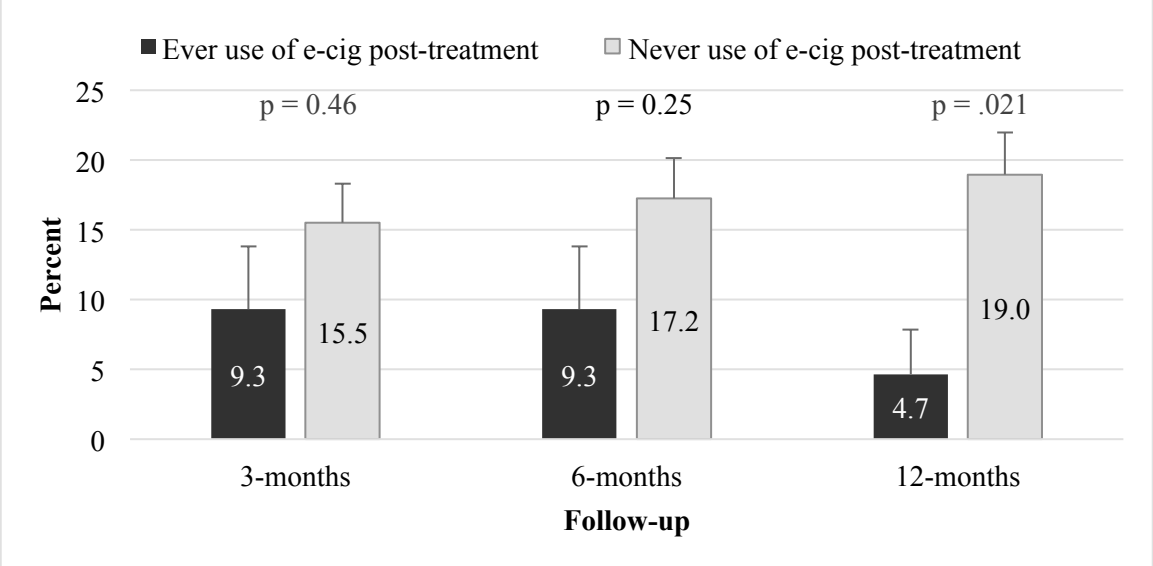
Figure 1. Percent of reported reasons for e-cigarette use at 3, 6, and 12 months.



E-cigarette Use and Tobacco Cessation

The association between e-cigarette use post-treatment and biochemically-confirmed tobacco abstinence at 3, 6, and 12 months is presented in Figure 2. At every follow-up, more participants who never used e-cigarettes post-treatment were tobacco abstinent compared to participants who used e-cigarettes post-treatment. This trend was not significant at 3 months (p=0.46) and 6 months (p=0.25), but was significant at 12 months (p=0.021). Specifically, four times as many never e-cigarette users were tobacco abstinent at 12-months, as compared to those who used e-cigarettes post-treatment (19.0% vs. 4.7%).

Figure 2. Percent abstinent (SEM) at 3, 6, and 12 months according to e-cigarette use post-treatment (n=217).



Adherence to the treatment protocol was not found to confound the association (Table 3). Use of e-cigarettes did not differ between the two conditions, face-to-face versus quit-line (p=0.49). In the face-to-face condition, there were no statistically significant differences between e-cigarette users and non-users in total number of in-person

counseling visits (p=0.66). While never users were more adherent to using nicotine patches, this difference was not significant at the 0.05 level (p=0.10). In the quit-line condition, there were no statistically significant differences between e-cigarette users and non-users in number of calls to the quit-line (p=0.53) and number of weeks of patches received (p=0.76).

Table 3. Adherence to counseling and medication by e-cigarette use post-treatment (n=217).

	Ever use of e-cig post- treatment	**Never use e-cig post- treatment**	***p* value**
Condition (%) (n=217)	(n=43)	(n=174)	
Face-to-Face	60.5	54.6	0.49
Quit-line	39.5	45.4	
Face-to-Face (n=121)	(n=26)	(n=95)	
Number of in-person counseling visits (Range 0-7)			
Mean ± SD	6.5 ± 0.91	6.4 ± 1.4	0.66
Number of patches used			
0-27	26.9	16.8	0.10
28-55	57.7	46.3	
56 or more	15.4	36.8	
Quit-line (n=96)	(n=17)	(n=79)	
Number of quit-line counseling calls,			
Mean ± SD	3.6 ± 2.7	3.2 ± 1.9	0.76
Number of weeks of patches received			
No weeks	11.8	16.5	0.99
2-4 weeks	35.3	34.2	
More than 4 weeks	52.9	49.4	

DISCUSSION

Among adult Appalachian smokers who were enrolled in a tobacco cessation trial, post-treatment e-cigarette users were less likely to achieve biochemically-validated abstinence at 12 months follow-up, as compared to non-users. This finding adds to the

growing number of observational studies[8,13,22-24] that have found that e-cigarette use decreases the likelihood that a smoker will successfully quit.

Past studies, including a recent meta-analysis published in the Lancet[23], have been criticized[32] for containing studies that assessed past e-cigarette use among current smokers and thus excluding people who used e-cigarettes and successfully stopped smoking. The strength of this study is that we examined e-cigarette use and abstinence among participants who intended to quit upon enrollment. This design therefore accounted for those who used e-cigarettes and then quit. Our results support past findings that e-cigarette use is associated with less success in quitting.

E-cigarette users did not differ from never users in their baseline smoking history, including nicotine dependence, quit attempts in the past year, and use of cessation aids in the past. Moreover, e-cigarette users did not appear to differentially engage in the tobacco cessation intervention. These findings contradict previous observational studies reporting that e-cigarette use is associated with greater nicotine dependence[13], higher number of past-year quit attempts[8], and use of more quit methods[8,13]. The reasons for these differences are not readily apparent but may be partially explained by lack of preventive services and cessation resources in this medically underserved area of the state[33,34]. While past studies have identified nicotine dependence and past NRT use as potential confounders in the association between e-cigarette use and tobacco cessation, our study does not support this idea.

The primary reasons cited for e-cigarette use included help in quitting and cutting down on cigarettes, and they are not as bad for health, all of which agree with previous findings[7-10]. These reasons resonate with marketing messages that e-cigarettes are less

harmful than traditional cigarettes and can help smokers to quit. Consumers have responded to these perceptions regardless of evidence. Additionally, an interesting result was that e-cigarette users at 3 months (end of treatment) reported many reasons for use, but at 6 and 12 months fewer participants reported each reason. Potentially, over time a regular pattern of e-cigarette behavior takes over, and the intent of quitting is replaced with the routine use of an additional product.

This study had several limitations. First, this study had a small sample size, as e-cigarette use questions were added to the baseline survey after the majority of participants had been enrolled. This late addition was prompted by the widespread marketing of e-cigarette products that was initiated after our study started.

Second, the follow-up question used to identify e-cigarette users at 3, 6, and 12 months post-treatment only screened for e-cigarette use in the past 7 days and thus potential e-cigarette users were likely missed. This may explain some of the lack of difference between groups, but suggests that perhaps the association between e-cigarette use and 12 month abstinence is underestimated.

Third, this study does not differentiate between type of e-cigarette device or the amount of nicotine in the device. Another limitation is the homogenous study population representing those trying to quit and living in Appalachian Ohio. On the other hand, this population is representative of those residing in a region characterized by a high prevalence of smoking[32]. Finally, the design was observational, which limits any causal inferences about e-cigarette use post-treatment for tobacco cessation.

Despite these limitations, this study adds to our limited understanding of e-cigarette use among a population that is seriously trying to quit smoking. It supports the growing

findings that e-cigarette users are less likely to successfully quit smoking. However, the effect of electronic cigarette use on smoking cessation remains controversial and lacks consensus. For example, policy experts in England are taking a harm-reduction approach and encouraging smokers to try vaping as their interpretation of findings suggests that smokers who use e-cigarettes are more likely to quit smoking [16,32,35].

Further high quality research studies are critically needed to determine the effect of e-cigarette use on smoking cessation. Given that e-cigarettes are not regulated or approved by the FDA, they cannot be tested via randomized controlled trials. Therefore, in the U.S., large, prospective cohort studies are needed. This evidence is essential for smokers to make informed decisions on whether to use e-cigarettes while trying to quit and to assist clinicians to effectively advise their patients about these products. Notably, the results will provide the FDA with evidence to assist in the development of appropriate regulatory actions, especially with regard to cessation claims surrounding e-cigarettes.

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REFERENCES

1. U.S. Department of Health and Human Services. The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General, 2014. http://www.surgeongeneral.gov/library/reports/50-years-of-progress/full-report.pdf. Accessed November 25, 2015.
2. Centers for Disease Control and Prevention. Current Cigarette Smoking Among Adults in the United States. http://www.cdc.gov/tobacco/data_statistics/fact_sheets/adult_data/cig_smoking/index.htm#national. Published December 8, 2015. Accessed December 15, 2015.
3. Centers for Disease Control and Prevention. Trends in Quit Attempts Among Adult Cigarette Smokers — United States, 2001–2013. *MMWR*. 2015; 64(40):1129-35.
4. U.S. Food and Drug Administration. (2014). Electronic Cigarettes (e-cigarettes). http://www.fda.gov/newsevents/publichealthfocus/ucm172906.htm. Accessed November 25, 2015.
5. Ayers JW, Ribisl KM, Brownstein JS. Tracking the rise in popularity of electronic nicotine delivery systems (electronic cigarettes) using search query surveillance. *Am J Prev Med.* 2011; 40(4): 448-453. doi:10.1016/j.amepre.2010.12.007
6. Richardson A, Ganz O, Vallone D. Tobacco on the web: Surveillance and characterization of online tobacco and e-cigarette advertising. *Tob Control.* 2014; 24(4): 341-347. doi:10.1136/tobaccocontrol-2013-051246
7. Rutten LJ, Blake KD, Agunwamba AA, et al. Use of E-cigarettes among current smokers: Associations among reasons for use, quit intentions, and current tobacco use. *Nicotine Tob Res.* 2015; 17(10): 1228-1234. doi:10.1093/ntr/ntv003
8. Vickerman KA, Carpenter KM, Altman T, Nash CM, Zbikowski SM. Use of electronic cigarettes among state tobacco cessation quitline callers. *Nicotine Tob Res.* 2013; 15(10): 1787-1791. doi:10.1093/ntr/ntt061
9. Grana RA, Popova L, Ling PM. A longitudinal analysis of electronic cigarette use and smoking cessation. *JAMA Int Med*. 2014; 174(5): 812-813. doi:10.1001/jamainternmed.2014.187

10. Richardson A, Pearson J, Xiao H, Stalgaitis C, Vallone D. (2014). Prevalence, harm perceptions, and reasons for using noncombustible tobacco products among current and former smokers. *Am J Public Health*. 2014; 104(8): 1437-1444. doi:10.2105/AJPH.2013.301804
11. Giovenco DP, Lewis MJ, Delnevo CD. Factors associated with e-cigarette use: A national population survey of current and former smokers. *Am J Prev Med*. 2014; 47(4): 476-480. doi:10.1016/j.amepre.2014.04.009
12. Pokhrel P, Fagan P, Little MA, Kawamoto CT, Herzog TA. Smokers who try e-cigarettes to quit smoking: Findings from a multiethnic study in Hawaii. *Am J Public Health.* 2013; 103(9): 57-62. doi:10.2105/AJPH.2013.301453
13. Pearson JL, Stanton CA, Cha S, Niaura RS, Luta G, Graham AL. E-cigarettes and smoking cessation: Insights and cautions from a secondary analysis of data from a study of online treatment-seeking smokers. *Nicotine Tob Res*. 2015; 17(10):1219-1227. doi:10.1093/ntr/ntu269
14. Bullen C, Howe C, Laugesen M, et al. Electronic cigarettes for smoking cessation: A randomised controlled trial. *Lancet.* 2013; 382(9905): 1629-1637. doi:10.1016/S0140-6736(13)61842-5
15. Caponnetto P, Campagna D, Cibella F, et al. EffiCiency and safety of an eLectronic cigAreTte (ECLAT) as tobacco cigarettes substitute: A prospective 12-month randomized control design study. *PloS One.* 2013; 8(6): 66317. doi:10.1371/journal.pone.0066317
16. Brown J, Beard E, Kotz D, Michie S, West R. Real-world effectiveness of e-cigarettes when used to aid smoking cessation: a cross-sectional population study. *Addiction.* 2014; 109(9): 1531-40. doi: 10.1111/add.12623.
17. Bullen C, McRobbie H, Thornley S, Glover M, Lin R, Laugesen M. Effect of an electronic nicotine delivery device (e cigarette) on desire to smoke and withdrawal, user preferences and nicotine delivery: Randomised cross-over trial. *Tob Control.* 2010; 19(2): 98-103. doi:10.1136/tc.2009.031567
18. Dawkins L, Turner J, Hasna S, Soar K. The electronic-cigarette: Effects on desire to smoke, withdrawal symptoms and cognition. *Addict Behav.* 2012; 37(8): 970-973. doi:10.1016/j.addbeh.2012.03.004

19. Dawkins L, Turner J Roberts A, Soar K. 'Vaping' profiles and preferences: An online survey of electronic cigarette users. *Addiction*. 2013; 108(6): 1115-1125. doi:10.1111/add.12150
20. Etter J, Bullen C. A longitudinal study of electronic cigarette users. *Addict Behav.* 2014; 39(2): 491-494. doi:10.1016/j.addbeh.2013.10.028
21. Polosa R, Caponnetto P, Morjaria JB, Papale G, Campagna D, Russo C. Effect of an electronic nicotine delivery device (e-cigarette) on smoking reduction and cessation: A prospective 6-month pilot study. *BMC Public Health*. 2011; 11, 786-2458-11-786. doi:10.1186/1471-2458-11-786
22. Grana R, Benowitz N, Glantz SA. E-cigarettes: A scientific review. *Circulation*. 2014; 129(19): 1972-1986. doi:10.1161/CIRCULATIONAHA.114.007667
23. Kalkhoran S, Glantz SA. E-cigarettes and smoking cessation in real-world and clinical settings: a systematic review and meta-analysis. *Lancet Respir Med.* 2016; doi:S2213-2600(15)00521-4
24. Borderud SP, Li Y, Burkhalter JE, Sheffer CE, Ostroff JS. Electronic cigarette use among patients with cancer: Characteristics of electronic cigarette users and their smoking cessation outcomes. *Cancer.* 2014; 120(22): 3527-3535. doi:10.1002/cncr.28811
25. National Institute on Drug Abuse. FAQs - Clinical Studies Involving Electronic Cigarettes and INDs. http://www.drugabuse.gov/researchers/research-resources/faqs-clinical-studies-involving-electronic-cigarettes-inds. Published November, 2014. Accessed December 15, 2015.
26. Fiore MC, Jaén CR, Baker TB, et al. *Treating Tobacco Use and Dependence: 2008 Update.* Clinical Practice Guideline. 2008; Rockville, MD: U.S. Department of Health and Human Services. Public Health Service. May 2008. doi:10.1016/j.amepre.2008.04.009
27. Heatherton TF, Kozlowski L, Frecker R, Fagerström KO. Fagerström Test for Nicotine Dependence: a revision of the Fagerström Tolerance Questionnaire. *Brit J Addiction*. 1991; 86(9): 1119-1127. doi:10.1111/j.1360-0443.1991.tb01879.x

28. Velicer WF, DiClemente CC, Prochaska JO, Brandenberg N. A decisional balance measure for assessing and predicting smoking status. *J Pers Soc Psychol.* 1985; 48(5): 1279-1289. doi:10.1037/0022-3514.48.5.1279
29. Velicer WF, DiClemente CC, Rossi JS, Prochaska JO. Relapse situations and self-efficacy: An integrative model. *Addict Behav.* 1990; 15(3): 271-283. doi:10.1016/0306-4603(90)90070-E.
30. SRNT Subcommittee on Biochemical Verification. Biochemical verification of tobacco use and cessation. *Nicotine Tob Research.* 2002; 4(2): 149-159. doi:1080/14622200210123581
31. Wewers ME, Shoben A, Conroy S, et al. (under review) Effectiveness of two community health worker models of tobacco dependence treatment among community residents of Ohio Appalachia. *Nicotine Tob Research*.
32. Science Media Centre. Expert reaction to meta-analysis looking at e-cigarette use and smoking cessation. http://www.sciencemediacentre.org/expert-reaction-to-meta-analysis-looking-at-e-cigarette-use-and-smoking-cessation/. Published January 14, 2016. Accessed January 31, 2016.
33. Bureau of Health Professions. Area resource file (ARF). Rockville, MD: U.S. Department of Health & Human Services. Health Resources and Services Administration, Bureau of Health Professions; 2005.
34. Halverson JA. An analysis of disparities in health status and access to health care in the Appalachian region. 2004. http://www.arc.gov/research/researchreportdetails.asp?REPORT_ID=82. Accessed July 15, 2014.
35. West R. Estimating the population impact of e-cigarettes on smoking cessation and smoking prevalence in England. 2015. http://www.smokinginengland.info/sts-documents/ Accessed April 24, 2015.